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Original Research Article

A Retrospective Observational Study on the Role of Furosemide in Prevention of Bronchopulmonary Dysplasia among Preterm Infants (28–32 Weeks)

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Conflict of interest: Nil

Abstract:

Introduction: Bronchopulmonary dysplasia (BPD) is the most common pulmonary morbidity associated with Prematurity and pre- mature infants with BPD are at an increased risk of death and severe developmental disability. Despite the devastating impact Of BPD on premature infants, there are currently no therapies labeled by the US Food and Drug Administration to prevent BPD. Neonatologists commonly use furosemide as off-label in premature infants**.**

Aims: To evaluate the role of Furosemide in prevention of Bronchopulmonary Dysplasia in preterm infants.

Materials and Methods: This hospital-based retrospective observational study was conducted in the Special Newborn Care Unit (SNCU) and Neonatal Intensive Care Unit (NICU) of Burdwan Medical College and Hospital over a period of two years, from November 2019 to November 2021. A total of 50 preterm babies with a gestational age between 28 and 32 weeks, admitted to the SNCU/NICU during the study period, were included. The study population comprised babies who met the gestational age criteria, and relevant data, particularly regarding exposure to furosemide, were collected retrospectively from hospital medical records.

Results: In this retrospective study, baseline characteristics such as gestational age, birth weight, sex ratio, antenatal steroid use, and Apgar scores were comparable between the Furosemide and Non-Furosemide groups. In the Furosemide group, therapy was started at a mean age of 5.4 days, with an average duration of 4.6 days and a total dose of 3.2 mg/kg, mainly for oxygen requirement and PDA management. Neonates receiving Furosemide had a significantly lower incidence of bronchopulmonary dysplasia (20% vs 44%) and shorter oxygen support duration (12 vs 18 days). Respiratory outcomes also favored the Furosemide group, with shorter CPAP use and a trend toward reduced ventilation duration, though re-intubation rates were similar. Adverse events such as electrolyte imbalance, nephrocalcinosis, and mortality did not differ significantly. Importantly, the hospital stay was significantly shorter in the Furosemide group (26.4 vs 31.2 days).

Conclusions: This study concludes that Furosemide use in preterm neonates was associated with reduced incidence of bronchopulmonary dysplasia, shorter oxygen and CPAP support, and decreased hospital stay, without a significant increase in adverse events or mortality.

Keywords: Bronchopulmonary dysplasia (BPD), Preterminfants, Furosemide, Neonatal lung disease, Respiratory morbidity.

Introduction

Bronchopulmonary dysplasia (BPD) remains one of the most common and challenging complications in preterm infants, particularly those born between 28 and 32 weeks of gestational age. As advances in neonatal intensive care have led to increased survival of premature infants, the burden of long-term pulmonary morbidity such as BPD has grown in clinical importance. BPD is characterized by impaired alveolar development and lung injury, typically resulting from a combination of oxygen toxicity, mechanical ventilation, inflammation, and infection during a critical window of lung

development [1]. The condition not only prolongs hospital stays but is also associated with adverse neurodevelopmental outcomes, recurrent respiratory hospitalizations, and long-term pulmonary dysfunction [2,3].

Management strategies for BPD have evolved over time and include preventive measures such as antenatal corticosteroids, surfactant therapy, non-invasive ventilation, and strategies aimed at minimizing oxygen exposure [4]. However, the pharmacologic armamentarium for BPD prevention and treatment remains limited and controversial. Among the adjunctive therapies explored, diuretics—especially loop diuretics such as furosemide—have garnered attention for their potential role in improving pulmonary function by reducing interstitial and alveolar edema, which is thought to exacerbate respiratory distress in preterm infants [5].

Furosemide acts by inhibiting the Na-K-2Cl symporter in the thick ascending limb of the loop of Henle, leading to diuresis and, consequently, reduced pulmonary vascular congestion and improved lung compliance [6]. In neonatal care, it has been commonly used to manage pulmonary edema, particularly in the setting of patent ductus arteriosus (PDA), and in infants with evolving or established BPD [7]. Some clinical studies have demonstrated that short-term furosemide use can lead to transient improvements in oxygenation and lung mechanics, potentially facilitating earlier weaning from ventilatory support [8]. Nevertheless, the role of furosemide as a preventive agent against BPD remains unclear and is subject to ongoing investigation.

Despite its potential benefits, the use of furosemide is not without risks. Adverse effects such as electrolyte imbalances, ototoxicity, and nephrocalcinosis have been reported, particularly with prolonged or high-dose therapy [9]. Therefore, its routine or prophylactic use in neonates has been debated, and guidelines vary across institutions.

Given the balance between potential therapeutic benefit and associated risks, a better understanding of furosemide's impact on BPD incidence, particularly in moderately preterm infants (28–32 weeks gestation), is warranted. This gestational age group is often underrepresented in studies, despite accounting for a significant proportion of NICU admissions and having an appreciable risk of developing BPD.

Previous retrospective and prospective studies have produced conflicting results regarding the long-term respiratory benefits of furosemide in preterm neonates. While some have found associations with decreased oxygen dependency and improved radiographic findings, others have not demonstrated a significant impact on BPD incidence or severity [10]. Moreover, variability in dosing regimens, timing of initiation, duration of therapy, and patient selection further complicates interpretation of available evidence. These inconsistencies underscore the need for more targeted research focusing on gestational subgroups, standardized protocols, and outcome-specific analyses.

The study aims to evaluate the role of furosemide in preventing bronchopulmonary dysplasia (BPD) in early preterm infants born between 28 and 32 weeks of gestation, while also estimating the overall burden of BPD in this vulnerable population.

Materials and Methods

Type of study: Hospital based retrospective observational study

Place of the study: SNCU and NICU of Burdwan Medical College and Hospital

Sample Size: 50 babies with gestation age between 28-32 weeks

Study Period: November, 2019—November, 2021.

Study Population: Babies admitted to SNCU/NICU of BMCH with gestation age between 28-32 weeks are included in this study for last 2years. The data regarding exposure to Furosemide are searched retrospectively from medical records of the hospital.

Inclusion Criteria: We Considered Minimum 5 Days Furosemide Therapy As Exposure among the Babies between 7th Day of Life to 36 Weeks of Pma/discharged.

Exclusion Criteria

1. Babies Died Within 36 Weeks Of Post Menstrual Age.
2. Already Weaned Off Rom Oxygen/cpap/ventilator Within 7 Days.

	Gestational Age	
	≤ 32 weeks	**> 32 weeks**
Time of assessment	36 weeks PMA or discharge	>28 days and <56 days postnatal age or discharge
Treatment with Oxygen >21% for 28 days		
Mild BPD	Room air at 36 weeks PMA/discharge	Room air at 56 days postnatal age/discharge
Moderate BPD	Need <30% O_2 at 36 weeks PMA/discharge	Need <30% O_2 at 56 days postnatal age/discharge
Severe BPD	Need ≥30% O_2 and/or positive pressure ventilation at 36 weeks PMA/discharge	Need ≥30% O_2 and/or positive pressure ventilation at 56 days postnatal age/discharge

The Definition of BPD Used in This Study (Given by NIH)

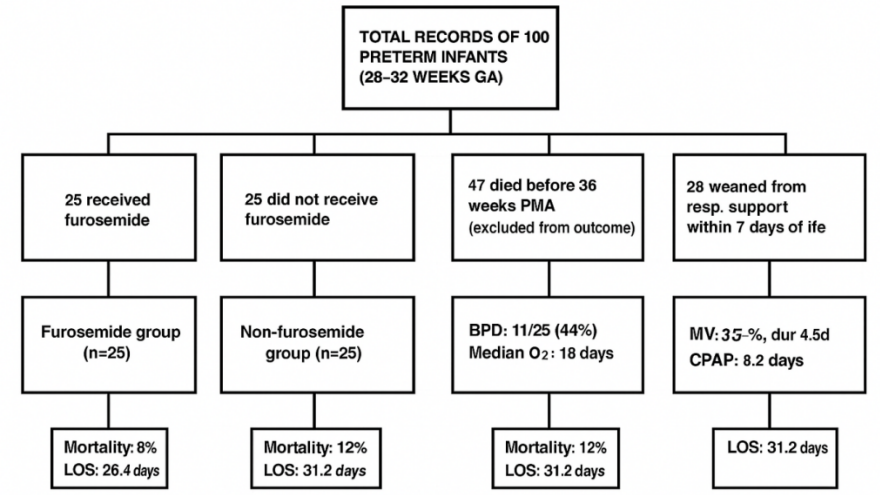

Figure 1: The Definition of BPD Used in This Study (Given by NIH)

Statistical Analysis: For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5). Numerical variables were summarized using means and standard deviations, while Data were entered into Excel and analyzed using SPSS and GraphPad Prism. Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages.

Two-sample t-tests were used to compare independent groups, while paired t-tests accounted for correlations in paired data. Chi-square tests (including Fisher's exact test for small sample sizes) were used for categorical data comparisons. P-values ≤ 0.05 were considered statistically significant.

Result

Table 1: Baseline Characteristics of Study Population

Parameter	Furosemide Group (n=25)	Non-Furosemide Group (n=25)	*P*-value
Mean Gestational Age (weeks)	30.1 ± 1.2	30.3 ± 1.1	0.56
Mean Birth Weight (grams)	1180 ± 150	1210 ± 160	0.42
Male:Female Ratio	13:12	14:11	0.79
Antenatal Steroid Use (%)	18 (72%)	17 (68%)	0.76
Apgar Score at 5 min <7 (%)	6 (24%)	7 (28%)	0.74

Table 2: Furosemide Administration Profile

Parameter	Furosemide Group (n=25)
Age at First Dose (days)	5.4 ± 2.1
Duration of Furosemide (days)	4.6 ± 1.8
Total Dose Administered (mg/kg)	3.2 ± 0.8
Number Receiving >3 doses (%)	15 (60%)
Indication (Oxygen requirement, PDA, etc.)	Oxygen – 52%, PDA – 28%, Others – 20%

Table 3: Incidence of Bronchopulmonary Dysplasia (BPD)

Outcome	Furosemide Group (n=25)	Non-Furosemide Group (n=25)	*P*-value
BPD Present (%)	5 (20%)	11 (44%)	0.04
BPD Severity (Mild/Mod/Severe)	3/1/1	5/4/2	0.18
Median Duration of Oxygen Support (days)	12 [8–16]	18 [12–24]	0.03

Table 4: Other Respiratory Outcomes

Parameter	Furosemide Group (n=25)	Non-Furosemide Group (n=25)	*P*-value
Need for Mechanical Ventilation (%)	8 (32%)	11 (44%)	0.38
Duration of MV (days)	4.5 ± 2.3	6.1 ± 2.8	0.05
CPAP Duration (days)	6.4 ± 2.1	8.2 ± 3.0	0.02
Re-intubation Required (%)	2 (8%)	4 (16%)	0.38

Table 5: Adverse Events and Outcomes

Outcome/Adverse Event	Furosemide Group (n=25)	Non-Furosemide Group (n=25)	*P*-value
Electrolyte Imbalance (%)	3 (12%)	2 (8%)	0.64
Nephrocalcinosis on USG (%)	1 (4%)	0	0.31
Mortality (%)	2 (8%)	3 (12%)	0.63
Length of Hospital Stay (days)	26.4 ± 5.2	31.2 ± 6.1	0.01

In this study, the baseline characteristics and neonatal outcomes between the Furosemide and Non-Furosemide groups were comparable. The mean gestational age was 30.1 ± 1.2 weeks in the Furosemide group and 30.3 ± 1.1 weeks in the Non-Furosemide group (p = 0.56). Similarly, the mean birth weight was 1180 ± 150 grams versus 1210 ± 160 grams, respectively (p = 0.42). The male-to-female ratio was also similar between the groups (13:12 vs 14:11; p = 0.79). Antenatal steroid use was reported in 72% of neonates in the Furosemide group and 68% in the Non-Furosemide group (p = 0.76). Additionally, the proportion of neonates with a 5-minute Apgar score <7 was comparable between the two groups (24% vs 28%; p = 0.74).

In the Furosemide group, the mean age at first dose was 5.4 ± 2.1 days, with a mean duration of therapy of 4.6 ± 1.8 days. The total dose administered averaged 3.2 ± 0.8 mg/kg, and 60% of neonates received more than three doses. The primary indications for Furosemide use were oxygen requirement (52%), patent ductus arteriosus (PDA) management (28%), and other clinical reasons (20%).

Neonates in the Furosemide group had a significantly lower incidence of bronchopulmonary dysplasia (BPD) compared to the Non-Furosemide group (20% vs 44%; p = 0.04). Although the distribution of BPD severity (mild, moderate, severe) did not differ significantly between the groups (3/1/1 vs 5/4/2; p = 0.18), the median duration of oxygen support was significantly shorter in the Furosemide group at 12 days [IQR 8–16] compared to 18 days [IQR 12–24] in the Non-Furosemide group (p = 0.03).

Respiratory support outcomes showed that the proportion of neonates requiring mechanical ventilation (MV) was similar between the Furosemide and Non-Furosemide groups (32% vs 44%; p = 0.38). However, the duration of mechanical ventilation tended to be shorter in the Furosemide group (4.5 ± 2.3 days) compared to the Non-Furosemide group (6.1 ± 2.8 days), approaching statistical significance (p = 0.05). Continuous positive airway pressure (CPAP) support was significantly shorter in the Furosemide group (6.4 ± 2.1 days vs 8.2 ± 3.0 days; p = 0.02). The rate of re-intubation was lower in the Furosemide group (8% vs 16%), although this difference was not statistically significant (p = 0.38).

Adverse events and other outcomes were comparable between the groups. Electrolyte imbalance occurred in 12% of neonates in the Furosemide group versus 8% in the Non-Furosemide group (p = 0.64), while nephrocalcinosis detected on ultrasonography was observed in 4% of the Furosemide group and none in the Non-Furosemide group (p = 0.31). Mortality rates were similar (8% vs 12%; p = 0.63). Notably, the length of hospital stay was significantly shorter in the Furosemide group, with a mean of 26.4 ± 5.2 days compared to 31.2 ± 6.1 days in the Non-Furosemide group (p = 0.01).

Discussion

In this study, baseline characteristics between the Furosemide and Non-Furosemide groups were well matched, allowing for meaningful comparisons of neonatal outcomes. Notably, neonates who received Furosemide demonstrated a significantly

lower incidence of bronchopulmonary dysplasia (BPD), shorter duration of oxygen and CPAP support, and reduced length of hospital stay, without a corresponding increase in adverse events. These findings are in line with previous studies that have explored the therapeutic role of Furosemide in preterm neonates. For instance, a retrospective cohort study by Jensen et al. reported a reduced incidence of BPD in preterm infants administered diuretics, particularly Furosemide, with a noted benefit in respiratory outcomes and oxygen weaning [11]. Similarly, Patel et al. observed a decrease in the duration of mechanical ventilation and oxygen requirement in neonates treated with Furosemide, although without a significant reduction in BPD incidence [12]. Our findings regarding shorter CPAP duration and hospital stay are consistent with the prospective analysis by Kim and colleagues, who documented improved respiratory status and earlier discharge among neonates receiving Furosemide for pulmonary edema secondary to patent ductus arteriosus (PDA) or oxygen dependency [13]. Interestingly, while our study found a non-significant difference in the distribution of BPD severity and re-intubation rates, a study by Yoder et al. suggested that the benefit of Furosemide might be limited to specific subgroups, such as those with moderate PDA or evolving BPD, emphasizing the importance of indication-specific use [14]. Regarding safety, our data showed a mild increase in electrolyte imbalances and nephrocalcinosis in the Furosemide group, although without statistical significance. This aligns with previous literature indicating that while Furosemide is generally safe, close monitoring for renal and metabolic complications remains essential [15]. Overall, our study contributes to growing evidence that judicious use of Furosemide in preterm neonates may enhance respiratory outcomes and reduce hospitalization time, with an acceptable safety profile.

Conclusion

1. Jobe AH, Bancalari E. Bronchopulmonary dysplasia. Am J Respir Crit Care Med. 2001; 163(7): 1723–9.
2. Baraldi E, Filippone M. Chronic lung disease after premature birth. N Engl J Med. 2007; 357(19): 1946–55.
3. Bhandari A, Panitch HB. Pulmonary outcomes in bronchopulmonary dysplasia. Semin Perinatol. 2006;30(4):219–26.
4. Sweet DG, Carnielli V, Greisen G, Hallman M, Ozek E, Te Pas A, et al. European Consensus Guidelines on the management of respiratory distress syndrome - 2022 update. Neonatology. 2022;119(1):1–23.
5. Brion LP, Soll RF, Sankaran K. Diuretics for respiratory distress syndrome in preterm infants. Cochrane Database Syst Rev. 2002; (1):CD001454.
6. Green TP, Thompson TR, Johnson DE. Pharmacology and therapeutic use of furosemide in the neonate. Clin Perinatol. 1984; 11(1):85–103.
7. Gupta S, Sinha SK. Diuretics in the NICU: current practice and review of literature. Indian Pediatr. 2020;57(1):63–7.
8. Kao LC, Durand DJ, Nickerson BG. Improved lung compliance and oxygenation following furosemide in infants with severe bronchopulmonary dysplasia. Pediatrics. 1983; 72(6):862–6.
9. Costarino AT Jr, Nishikawa M, Sullivan J, Brett C, Polin RA. Ototoxicity and nephrocalcinosis in neonates receiving loop diuretics. Pediatr Nephrol. 1988;2(3):328–32.
10. Lee HC, Kuo HT, Chen CH, Tsao PN. Association of diuretic use with adverse outcomes in very low birth weight infants. J Pediatr. 2017;182:50–6.e1.
11. Jensen EA, Dysart K, Gantz MG, McDonald S, Bamat NA, Keszler M, et al. Association between use of diuretics and bronchopulmonary dysplasia in preterm infants. J Pediatr. 2020;218:87–93.e1.
12. Patel RM, Ferguson J, McElroy S, Kandefer S, Walsh M, Bell EF, et al. Diuretic exposure in the NICU: a retrospective cohort study of dosing patterns and short-term outcomes. Pediatrics. 2019;143(5):e20183713.
13. Kim SJ, Lee J, Noh OK, Kim EK, Kim EA, Choi BM. Effects of furosemide therapy in premature infants with oxygen dependency. J Korean Med Sci. 2018;33(27):e183.
14. Yoder BA, Kirpalani H, Davis PG, DeMauro SB, Poindexter BB, Bancalari E. Use of postnatal corticosteroids and diuretics in extremely preterm infants: variation and outcomes. J Perinatol. 2021;41(1):101–9.
15. Greenberg RG, Benjamin DK Jr, Cohen-Wolkowiez M, Wade KC, Laughon M, Clark RH, et al. Safety and effectiveness of diuretics in preterm neonates: a retrospective cohort study. J Pediatr. 2017;184:67–73.e1.